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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/061,727	10/26/2001	John E. Sims	3151-A	9375

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EXAMINER
LI, RUIXIANG

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/061,727	SIMS ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cov r sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *3, 4, 8, and 12-14* is/are withdrawn from consideration.

5)☒ Claim(s) *1,7 and 11* is/are allowed.

6)☒ Claim(s) *5,6,9 and 10* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicants' election of Group I (claims 1, 2, 5, 6, 7, 9, 10, and 11), drawn to an isolated polynucleotide encoding a polypeptide of SEQ ID NO: 2, in Paper No. 7 filed on 04/08/2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

   The restriction requirement is made FINAL.

2. Claims 1-14 are pending. Claims 1, 2, 5 (in part), 6 (in part), 7, 9 (in part), 10 (in part), and 11, drawn to an isolated polynucleotide encoding a polypeptide of SEQ ID NO:2 are under consideration. All other claims are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to a provisional application, 60/244,831, filed on October 31, 2000.

Drawings

4. The drawing (Figure 1) filed on October 26, 2001 is accepted by the Examiner.

Rejections—35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 9 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 1 recites a host cell comprising an expression vector that comprises a nucleic acid molecule. Thus, the claim reads on a transgenic human, which is non-statutory subject matter. It is recommended that the term "an isolated host cell" be used to overcome this rejection.

Claim Rejections—35 USC § 112, 1st paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 5, 6, 9, and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide of SEQ ID NO: 1 or an isolated polynucleotide encoding a human interleukin-1 receptor accessory protein (IL-1R AcP) set forth in SEQ ID NO: 2, does not reasonably provide enablement for (i) a polynucleotide encodes a polypeptide comprising the asserted cytoplasmic domain of SEQ ID NO: 2 or its fragment; (ii) an isolated polynucleotide comprising an isolated nucleic acid molecule that hybridises to the polynucleotides of (i); (iii) an isolated polynucleotide comprising an isolated nucleic acid molecule that is

at least 85% identical to the polypeptides of (i) and (ii); and an isolated polynucleotide comprising a polynucleotide that is degenerate to any of the polynucleotides of (i)-(iii). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claim 5 is drawn to polynucleotides comprising (i) a polynucleotide that encodes a fragment of SEQ ID NO: 2 (the asserted cytoplasmic domain) or a fragment of the asserted cytoplasmic domain; (ii) an isolated nucleic acid molecule that hybridises to the polynucleotides; (iii) an isolated nucleic acid molecule that encodes a polypeptide that is at least 85% identical to the polypeptide comprising the asserted cytoplasmic domain of SEQ ID NO: 2 or a fragment of the asserted cytoplasmic domain; and (iv) a polynucleotide that is degenerate to any of the polynucleotides of (i)-(iii). Thus, the claim is so broad that it encompasses an enormous genus of huge number of nucleic acids that vary substantially both in length and in nucleotide composition. Claims 6, 9, and 10 depend from claim 1.

However, other than the nucleic acid sequence of SEQ ID NO: 1 that encodes

an IL-1R AcP protein of SEQ ID NO: 2, the disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. Despite the disclosure of the cytoplasmic domain of the IL-1R AcP protein, the disclosure does not show (i) which portions of SEQ ID NO: 1 are critical to the activity of the IL-1R AcP protein encoded by the claimed nucleic acid; and (ii) what modifications (e.g., substitutions, deletions or additions) one can make to SEQ ID NO: 1 will result in protein mutants with the same functions as the claimed protein. The state of the art (See, e.g., Ngo, et al, *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz, et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495) is such that the relationship between sequence of a protein and its activity is not well understood and is not predictable. Excising out portions of a protein or modifications to a protein, e.g., by substitutions or deletions, would often result in deleterious effects to the overall activity and effectiveness of the protein. It is noted that claim 1, part a, b, e, h and j, does not even require a specific functional limitation. It is further noted that, despite the presence of a functional limitation in claim 1, part g and I, the claim is still very broad because there the functional limitation, "a signal transduction factor" is broad because it encompasses any signal transduction factors and does not limit to the factors involved in the interaction of the IL-1R AcP with IL-1 receptor. Thus, the instant disclosure fails to enable one skilled in the art to make and/or use the claimed polynucleotides that encode various fragments and homologous of SEQ ID NO: 2.

Furthermore, the instant disclosure fails to make and use an isolated polynucleotide comprising an isolated nucleic acid molecule that hybridises to the

polynucleotides recited in claim 1, part a, b, e, and g without any functional limitations. The state of the art is such that determining the specificity of hybridization is empirical by nature and the effect of mismatches is unpredictable, as taught by Wallace et al. (Methods Enzymol. 152:432-443, 1987) and Sambrook et al. (Molecular Cloning, A Laboratory Manual, 2nd Edition, 1989, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, page 11.47).

Accordingly, the disclosure fails to enable such a myriad of the claimed nucleic acid molecules that not only vary substantially in length but also in nucleic acid composition and to provide any guidance to one skilled in the art on how to make and use the claimed genus of nucleic acid molecules. Thus, it would require undue experimentation for one skilled in the art to make and use the claimed genus of the molecules embraced by the instant claims.

Claim Rejections—35 USC § 112, 1st paragraph

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 5, 6, 9, and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification discloses human interleukin-1 receptor accessory protein (IL-1R AcP) set forth in SEQ ID NO: 2 and polynucleotides encoding the proteins set

forth in SEQ ID NO: 1. The native human IL-1R AcP includes a polymorphism that is present at about a 50/50 ratio. The polymorphism exists as an A at position 1792 of SEQ ID NO: 1, or a C at position 1792 of SEQ ID NO: 1. This results in a Thr at position 598 of SEQ ID NO: 2, or a Pro at position 598 of SEQ ID NO: 2. The specification further discloses that the IL-R AcP polypeptides and polynucleotides of this invention are an alternatively spliced variant of IL-1R AcP in which part of the C-terminal of the cytoplasmic domain is relaced by an alternative peptide sequence. At least part of this alternative peptide sequence is amino acids 449-687of SEQ ID NO: 2 (page 6 of the specification). The disclosure also discloses two additional preferred fragments of SEQ ID NO: 2, amino acids 384-687 of SEQ ID NO: 2 and amino acids 379-687 of SEQ ID NO: 2, which applicants assert are capable of interacting with a signal transduction factor (pages 9 to 10).

However, claim 5 (part g) recites an isolated polynucleotide comprising a polynucleotide that encodes a fragment of the cytoplasmic domains as recited in claim 1, part a, b, and e; claim 5 (part h) recites an isolated polynucleotide comprising an isolated nucleic acid molecule that hybridises to the polynucleotides recited in claim 1, part a, b, e, and g; claim 5 (part i) recites an isolated polynucleotide comprising an isolated nucleic acid molecule that encodes a polypeptide that is at least 85% identical to the polypeptides described in claim 1, part a, b, e, and g; claim 5 (part j) recites an isolated polynucleotide comprising a polynucleotide that is degenerate to any of the polynucleotides of recited in claim 1, part a, b, e, g, and i. Thus, the claim encompasses an enormous genus of huge number of nucleic acids that vary substantially both in length and in nucleic acid composition. Claims 6, 9, and

10 depend from claim 1.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim 1, part a, b, and e, is a recitation of the cytoplasmic domains; claim 1 (part a, b, and e) does not require that the nucleic acids possess any particular biological activity. Furthermore, claim 1 (part h and j) does not even require that the nucleic acids possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. There is not even identification of any particular portion of the structure that must be conserved. While claim 1, part g and I has a functional limitation, "a signal transduction factor", such a limitation is broad because it encompasses any signal transduction factors and does not limit to the factors involved in the interaction of the IL-1R AcP with IL-1 receptor. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize

that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, only the isolated polynucleotides encoding IL-1R AcP of SEQ ID NO: 2 (including SEQ ID NO: 1), but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections—35 USC § 112, 2nd paragraph

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is indefinite because it (part g and part i) recites "polypeptide(s) described in a)-g)". Claim 1 (part a and part g) recites a polynucleotide, not a

polypeptide or a fragment of polypeptide. Thus, the recitation in part g and part I of claim 1 is confusing and makes the claim indefinite.

Claim Rejections—35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 5 (part h), 6, 9, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Huang et al. (Recruitment of IRAK to the interleukin 1 receptor complex requires interleukin 1 receptor accessory protein. *Proc. Natl. Acad. Sci. USA* 94:12829-12832, 1997).

Huang et al. teach a cDNA, which encodes a interleukin 1 receptor accessory protein. This cDNA encodes amino acid residues 1 to 448 of SEQ ID NO: 2, comprising amino acid residues 384 to 484 of SEQ ID NO: 2 which is a portion of the polypeptide frgments recited in claim 5 (See attached sequence alignment). Thus, this cDNA would, by its nature, hybridize to the polynucleotides recited in claim 1 (part a-g). Huang et al. further teach an expression vector (pFlag-CMV-1) comprising the cDNA, hosct cells comprising the vector, and expression of the protein in cultured

mammalian cells, e.g., 293 cells (right column of page 12829). Thus, the reference of Huang et al. meets the limitations of claims 5 (part h), 6, 9, and 10.

16. Claims 5 (part h), 6, 9, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Cao (US Patent No. 6,280,955, August 28, 2001; 102 (e) date: December 16, 1997).

Cao teaches a cDNA, which encodes a interleukin 1 receptor accessory protein. This cDNA encodes amino acid residues 1 to 448 of SEQ ID NO: 2, comprising amino acid residues 384 to 484 of SEQ ID NO: 2 which is a portion of the polypeptide frgments recited in claim 5 (See attached sequence alignment). Thus, this cDNA would, by its nature, hybridize to the polynucleotides recited in claim 1 (part a-g). Cao further teaches an expression vector comprising the cDNA (pFlag-CMV-1), hosct cells comprising the vector, and expression of the protein in cultured mammalian cells, e.g., 293 cells (Examples; bottom of column 7 to top of column 8). Thus, the reference of Cao meets the limitations of claims 5 (part h), 6, 9, and 10.

Claim Objections—Minor Informalities

17. Claim 2 is objected to because the period "." Is missing at the end of the claim.

Claims 5, 6, 9, and 10 are objected to because they recite unelected subject matter, polynucleotides encoding polypeptides comprising fragments of SEQ ID NO: 4.

Claim 5 is objected to because part g) refers itself (a-g).

Claim 9 is objected to because it appears that it depends from claim 6, not claim 5.

Appropriate correction is required.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday-Friday, 8:30 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ruixiang Li
Examiner
May 24, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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